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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,001	09/30/2004	Masayuki Amagai	4439-4025	3825

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,001	AMAGAI ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4 are pending.

For examination purposes, the claimed recitation is read as a composition or formulation comprising a CD40L antagonist (e.g., see page 9, paragraph 2 of the instant specification).

2. Applicant is invited to claim the benefit of priority to the prior-filed application PCT/JP03/04219 in the first sentence(s) of the specification following the title.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Note that the proper designation of 'cdl" is "CD40L".

Note the antagonist should be spelled "antagonist"

Further, given the rejections under 35 USC 112, first paragraph, herein; applicant is invited to limit the claimed CD40L antagonist in the Title to anti-CD40L antibodies.

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

5. Claims 1-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 are indefinite in the recitation of "a CD40L receptor" and "a CD40 receptor" because the nature of these receptors is ambiguous.

For example, the claimed recitation of "a CD40L receptor" is ambiguous because it is unclear whether the intent is to read on "CD40L itself" or to a molecule that is a receptor for CD40L (e.g., anti-CD40L antibody, CD40).

Applicant is invited to amend the claims to recite "CD40L" and "CD40", if this is applicant's intent.

If applicant intends the claims to read on a molecule that binds CD40L/CD40 (e.g., a receptor for CD40L/ CD40), then applicant should amend the claims to clearly indicate that "CD40L receptor and CD40 receptor" are something other than CD40L and CD40 themselves.

Also, note that claims 2 and 4 recite "anti-CD40L antibody" and do not recite anti-CD40L receptor antibody".

For examination purposes, the recitation of CD40L receptor and CD40 receptor read on CD40L and CD40 themselves, which appears consistent with the instant specification as filed (e.g., see pages 6-7 of the instant specification).

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 3-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting various inflammatory conditions with CD40L- specific antibodies accurately reflects the relative ability or efficacy of the claimed "preventative agents" to prevent pemphigus.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.
See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively prevent pemphigus by administering CD40L-specific antibodies / CD40L antagonists. The specification does not teach how to extrapolate data obtained from various in vitro or in vivo observations as well as clinical experience with CD40L-specific antibodies / CD40L antagonists to the development of effective methods of preventing pemphigus in humans broadly encompassed by the claimed invention.

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human disorders or diseases such as pemphigus targeted by the claimed "preventative agents". With respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed only after significant tissue damage has occurred.

For example, The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) indicates that:
Pemphigus is a serious disease with an inconsistent and unpredictable response to therapy and that the aim of treatment is to stop the eruption of new lesions.
See Treatment on page 829.

Therefore, the treatment of pemphigus is drawn to the treatment of the disease and its associated lesions subsequent to an individual being diagnosed with pemphigus and not as a preventative agent of the disease itself, as recited in the current claims.

There is insufficient guidance and direction as well as objective evidence to provide for preventing pemphigus recited in the instant claims.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to prevent pemphigus with therapeutic agents, undue experimentation would be required to practice the claimed "preventative agents" to prevent pemphigus with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed "preventative agents" and absent working examples providing evidence which is reasonably predictive that the claimed "preventative agents" are effective for preventing pemphigus encompassed by the claimed products.

Applicant is invited to amend the claims to avoid the recitation of "prevention".

8. Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim is drawn to an "antagonist that inhibits the interaction between CD40L receptor mediating the contact-dependent helper effector function on the T cell surface and a CD40 receptor on the antigen-presenting cell surface".

Such "antagonists" do not meet the written description provision of 35 USC 112, first paragraph. There is insufficient guidance and direction as to the written description of these "antagonists", as broadly encompassed by the claimed invention.

While pages 6-7 of the instant specification appears to disclose the known anti-CD40L antibodies, soluble CD40 and soluble CD40L as "antagonists",
the instant application has not provided a sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus of "antagonists that inhibit the interaction between CD40L receptor mediating the contact-dependent helper effector function on the T cell surface and a CD40 receptor on the antigen-presenting cell surface".

Even with disclosing the known CD40L antagonists, the instant disclosure does not distinguish between monomeric CD40L, which is considered an antagonist and oligomeric CD40L, which is considered an agonist.
For example, see Armitage et al. (U.S. Patent No. 6,264,951), which teaches antagonistic soluble monomeric CD40L (versus agonistic oligomeric CD40L) and soluble CD40 capable of blocking and preventing CD40L:CD40 interactions, including their use in therapy (e.g., see column 10, paragraph 3 – column 11, paragraph 1).

Given the broad structural and functional differences between the CD40L antagonists as "antagonists" or "agents", including those disclosed on page 6 of the instant specification as-filed.
there is insufficient written description of the broadly recited "antagonists" or "agents" in the absence of a sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure.

Further, the Court has interpreted 35 U.S.C. §112, first paragraph, to require the patent specification to "describe the claimed invention so that one skilled in the art can recognize what is claimed. Enzo Biochem, Inc. v. Gen-Probe Inc, 63 USPQ2d 1609 and 1618 (Fed. Cir. 2002). In evaluating whether a patentee has fulfilled this requirement, our standard is that the patent's "disclosure must allow one skilled in the art 'to visualize or recognize the identity of' the subject matter purportedly described." Id. (quoting Regents of Univ. of Cal. v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed Cir. 1997)).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483.

Applicant has been reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Therefore, there is insufficient written description for "antagonists" or "agents" other than that disclosed in the specification as filed under the written description provision of 35 USC 112, first paragraph.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Black et al. (U.S. Patent No. 6,001,358) (see entire document).

Black et al. teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see columns 34-38) as well as their use in the inhibition of CD40L:CD40-mediated interactions, including the treatment of autoimmune and non-autoimmune conditions (e.g., see columns 31-34), including pemphigus (e.g., see column 33, lines 4-5) (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antagonistic anti-CD40L antibodies and therapeutic compositions thereof.

11. Although the claims do not recite therapeutic antagonistic soluble monomeric CD40L and soluble CD40 capable of blocking and preventing CD40L:CD40 interactions per se,
the following rejection has been applied to advance prosecution to show that the other known CD40L antagonists at the time the invention was made, namely soluble monomeric CD40L and soluble CD40 were known in the art at the time the invention was made and consistent with the disclosure on page 6, paragraph 1 of the instant specification as filed.

Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as being anticipated by Armitage et al. (U.S. Patent No. 6,264,951) (see entire document).

Armitage et al. teach antagonistic soluble monomeric CD40L and soluble CD40 capable of blocking and preventing CD40L:CD40 interactions, including their use in therapy (e.g., see column 10, paragraph 3 – column 11, paragraph 1), including compositions thereof (e.g., see column 21, paragraph 1) (see entire document, including Detailed Description of the Invention). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. Although the prior art does not teach the intended use of such antagonists for pemphigus per se, the claimed functional limitations would be inherent properties of the referenced antagonistic soluble CD40L and soluble CD40 and compositions thereof.

A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Also, see MPEP 2111.02

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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March 24, 2007